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Rewarming Mice from Hpothermia by Exposure to 2450-MHz Microwave Radiation

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16. ABSTRACT

Radiofrequency (RF) radiation between frequencies of 1 MHz and 100 GHz is, to varying degrees, readily transmitted and absorved in biolocical tissues (8). Because of its internal absorption characteristics, RF radiation in the microwave spectrum (300-10,000 MHz) has been used in cases where a rapid rate of warming is desired without raising actual temperature beyond lethal levels. For example, microwave exposure has been used to quickly thaw canine kidneys (5), warm human blood from 4 to 37 C in 1 min (10), and selectively warm the cardiac area of hypothermic rats (1,2). It is conceivable that whole-body exposure to RF radiation could be used in the rewarming of subjects in experimental or accidental hypothermia. Warm-water baths have conventionally been used for rewarming hypothermic individuals, however, this method is relatively slow and can lead to ill effects such as hypoglycemia (6) and reductions in arterial blood pressure (6). With RF exposure all of the tissues can simultaneously be warmed at rates far greater than possible with convective, conductive, and/or infrared heating. Early reports have indicated that internal microwave heating is more beneficial than external heating for reviving rats from hypothermia (2). Thus, microwave radiation can be used to rewarm hypothermic subjects; however, it is not known what internal heating rate a mammal can endure during recovery from hypothermia.

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Rewarming Mice from Hypothermia by Exposure to 2450-MHz Microwave Radiation

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Radiofrequency (RF) radiation between frequencies of 1 MHz and 100 GHz is, to varying degrees, readily transmitted and absorbed in biological tissues (8). Because of its internal absorption characteristics, RF radiation in the microwave spectrum (300–10,000 MHz) has been used in cases where a rapid rate of warming is desired without raising actual temperature beyond lethal levels. For example, microwave exposure has been used to quickly thaw canine kidneys (5), warm human blood from 4 to 37°C in 1 min (10), and selectively warm the cardiac area of hypothermic rats (1, 2).

It is conceivable that whole-body exposure to RF radiation could be used in the rewarming of subjects in experimental or accidental hypothermia. Warm-water baths have conventionally been used for rewarming hypothermic individuals, however, this method is relatively slow and can lead to ill effects such as hypoglycemia (6) and reductions in arterial blood pressure (6). With RF exposure all of the tissues can simultaneously be warmed at rates far greater than possible with convective, conductive, and/or infrared heating. Early reports have indicated that internal microwave heating is more beneficial than external heating for reviving rats from hypothermia (2). Thus, microwave radiation can be used to rewarm hypothermic subjects; however, it is not known what internal heating rate a mammal can endure during recovery from hypothermia.

Until recently it was not possible to measure tissue temperature during microwave exposure because of the electric field perturbations of RF radiation on metallic conductors. However, with the recent development of nonperturbing temperature probes and waveguide exposure systems that permit accurate dosimetry of absorbed RF energy, it is now possible to rewarm hypothermic animals and determine maximum tolerable heating rates. In this study the effects of deep-body heating rate on the survivorship of hypothermic mice exposed to whole-body 2450-MHz microwave radiation are assessed.

MATERIALS AND METHODS

The animals used in this study were adult male AJ and CD-1 albino mice with a range in body weight of 25–40 g (31.2 ± 4.1 g; $\bar{X}$ ± SD). The mice were housed at an ambient temperature of 22°C, 12:12 L:D photoperiod, and given rat chow and water *ad libitum*.

Exposure System

The animals were exposed to whole-body 2450-MHz microwave radiation inside a rectangular waveguide (5.8 × 11.2 × 30.5 cm). The schematic in Fig. 1 shows the path of the microwaves through the exposure system. As the microwaves pass through the waveguide there is a small but constant loss in power (~16%) due to leakage and attenuation in the cables and electrical con-

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nectors, and absorption and scattering by the plastic animal holder. When a mouse (or any biological material) is placed in the microwave field, a relatively large drop in power will be detected at the output of the waveguide (i.e., P_{tran} in Fig. 1). By measuring the power of the radiation entering (P_{inc}) and leaving the waveguide (P_{tran}) and the reflected power (P_{ref}) that emits from the mouse back to the microwave generator, the power absorbed by the mouse can be calculated ($P_{abs} = P_{inc} - P_{tran} - P_{ref}$). Absorbed power is continuously recorded by summing the analog voltage outputs from the power meters depicted in Fig. 1. In this study power absorption per unit body weight is defined as the specific absorption rate (SAR, W kg^{-1}).

Protocol

A mouse was restrained in a perforated plastic tube oriented longitudinally with respect to the long axis of the waveguide. A Vitek temperature probe (Model No. 101) designed to provide unperturbed measurements of temperature in a RF radiation field (30 to 3000 MHz) was inserted approximately 20 mm past the anal sphinctor and secured to the tail with adhesive tape. Because metal will heat as well as severely perturb the field during microwave exposure, conventional physiological monitoring devices cannot be placed on an animal during RF exposure.

The waveguide, excluding the electrical connections, was immersed in an ice-water

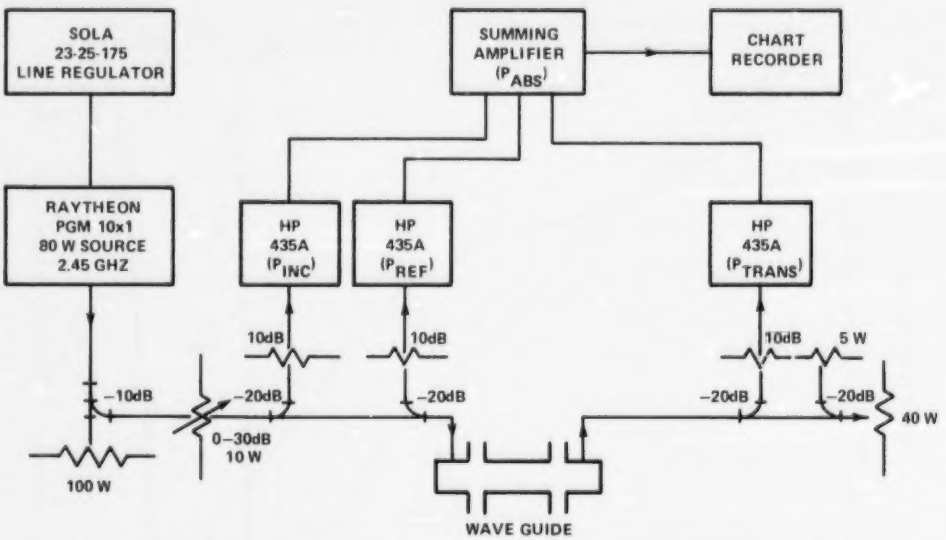

FIG. 1. Schematic of the path of microwaves through the 2450-MHz waveguide exposure system. Ninety percent of the power from the generator is routed to a 100-W termination load while the remaining power is passed through a 0- to 30-db variable attenuator and then into the waveguide. Hewlett-Packard 453A power meters are used to monitor the incident (P_{inc}), reflected (P_{ref}), and transmitter power (P_{tran}) emitting to and from the waveguide. Microwave power not absorbed by the mouse is passed to the terminal load. For P_{inc} exposures above 40 W the 10-db coupler and 30-db attenuator (lower left corner) were bypassed and the termination load was increased from 40 to 100 W. A chart recorder continually monitors absorbed power which is derived by integrating the analog voltages from the power meters. The voltage line regulator is optional. The waveguide exposure system is modified from that of Ho and Edwards (4).

bath. Fresh air was continuously circulated through the waveguide. The restrained mouse with attached temperature probe was placed in the waveguide while deep-body temperature was continuously recorded on a chart recorder.

The mice were cold-exposed until body temperature decreased to an average of 25.7 ± 4.8°C ($\bar{X}$ ± SD). A wide range of temperature (17–30°C) was used in order to evaluate the ability of microwave radiation to successfully recover mice from relatively shallow to very deep hypothermia. Approximately 30–60 min of cold exposure was required to reach the desired hypothermic state; at which time the microwave generator was activated and incident powers of 10 to 80 W were directed into the waveguide. Microwave exposure was terminated when body temperature recovered to the precold exposure level ($T_b \approx 37$°C). The mouse was quickly removed from the waveguide, weighed, and observed for any obvious changes in coordination and signs of microwave burns, and then returned to its cage. The mice were observed for at least 1 week following microwave exposures for any delayed signs of microwave burns and/or any obvious health symptoms. Each mouse ($N = 19$) was exposed once to cold and microwave rewarming.

RESULTS

Placing the mice in the cold waveguide resulted in a linear reduction in body temperature at a rate of approximately 0.2°C/min (Fig. 2). Rewarming the hypothermic mice to normothermia by exposure to

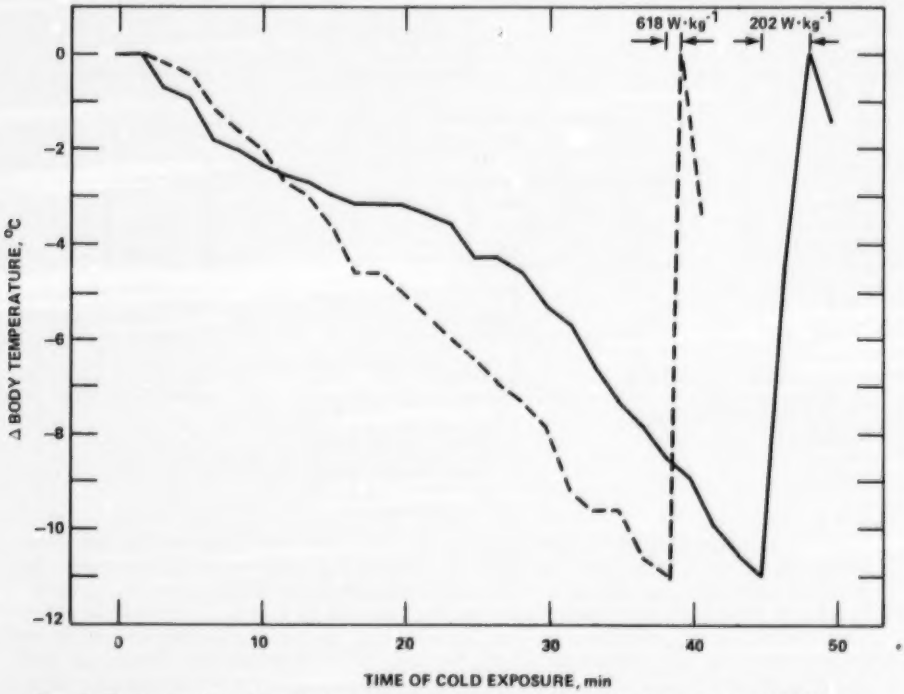

FIG. 2. Two examples of rewarming mice from deep hypothermia by exposure to 2450-MHz microwave radiation. Exposure to a whole-body SAR of 202 W/kg caused colonic temperature to increase by 0.057°C/sec; exposure to 618 W/kg raised colonic temperature by 0.28°C/sec.

2450-MHz microwaves was reached by increasing body temperature at average rates of 0.04 to as high as 0.65°C/sec. There was a slight parabolic relationship between heating rate and SAR (Fig. 3). At the termination of microwave exposure body temperature began to fall at a relatively rapid rate until the mice were removed from the waveguide (Fig. 2). This drop in temperature was attributed to rewarming the mice while maintained under cold-exposed conditions.

When removed from the plastic restrainer the mice usually displayed normal coordination. Only at the very high SARs did some of the mice show ataxia immediately after removal from the waveguide. In these ataxic mice their limbs and tails felt cold to the touch whereas the appendages of mice exposed at the lower SARs were noticeably warmer. All mice that initially displayed signs of ataxia regained normal coordination in less than 30 min after rewarming.

Microwave exposure caused burns at the base of the tails in some animals. Within 1 week postexposure to microwaves the tails of 12 of 19 mice were either severed at the base or were severely necrotic (e.g., entire tail colored black). Tail burning occurred at low as well as high SARs.

Other than tail burning, the cold and microwave exposure treatments apparently had no other ill effects on all but one of the mice. One mouse died 4 days after the rewarming experiment. This particular death may have been attributed to cold exposure rather than the microwave treatment since the body temperature of this animal was lowered to 16.9°C (lowest in group) while rewarming was made at a relatively low SAR of 290 W/kg.

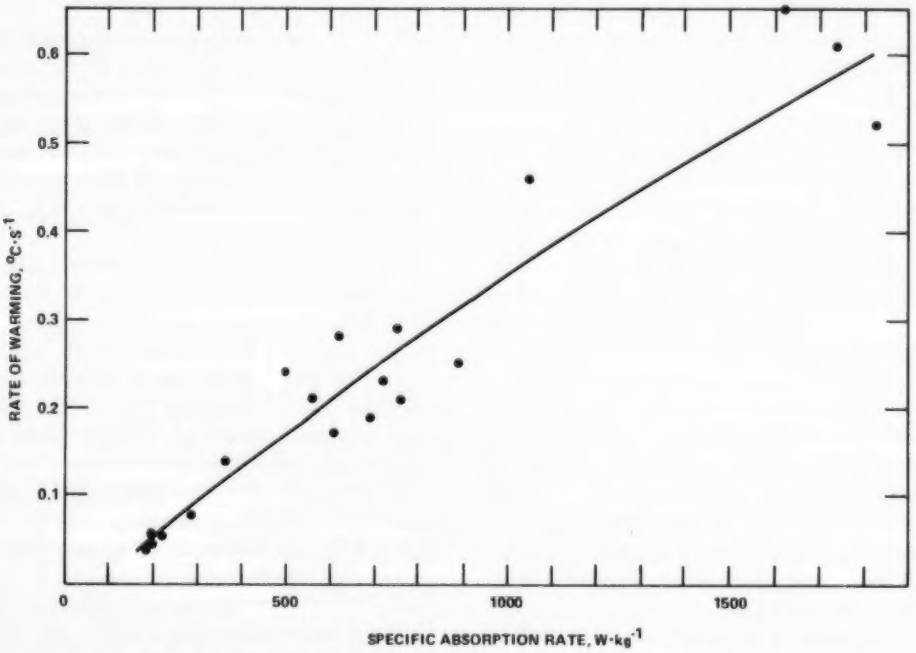

FIG. 3. Relationship between SAR and rate of increase in colonic temperature in hypothermic mice. Least-squares regression line fit with a parabolic equation, $Y = A + BX + CX^2$, where $A = -0.036$, $B = 4.3 \times 10^{-4}$, $C = -4.5 \times 10^{-8}$, and $R^2 = 0.9210$.

DISCUSSION

These data demonstrate that the internal tissues of the hypothermic mouse can tolerate temperature increments of 7 to 20°C at rates of at least 0.65°C/sec. The wavelength of 2450-MHz microwaves (12.2 cm) is resonant for a mass the size of a mouse (3). This electromagnetic resonance results in a heavy internal deposition of energy throughout the trunk or core of the animal. It should be noted that the SARs used in this study could not be tolerated for very long in a normothermic-exposed animal (i.e., T_b = 37°C). Only when rodents are maintained under extreme cold conditions can they tolerate large doses of microwave radiation (11).

Andjus *et al.* (2) reported on the beneficial effects of using 3000-MHz microwave radiation to rewarm rats from deep hypothermia (T_b = −6°C). The rate of rewarming during microwave radiation was approximately 0.013°C/sec, or 50 times slower than the maximum warming rates measured in the present study. In the experiments of Andjus *et al.* (2) and Andjus and Lovelock (1) a microwave beam was directed over the chest of the hypothermic rat which resulted in an initial warming of the cardiac area with little direct heating of the other deep body organs or skin. Once body temperature had reached 20°C the rat was removed from the microwave source and immersed in a 40°C water bath to complete the rewarming process. Conductive or infrared heating of the chest was less effective for promoting recovery from hypothermia; 20 and 68% survivorship, respectively, compared to 100% survival in the animals rewarmed with microwaves (2). Cardiovascular function is improved when anesthetized, hypothermic dogs were rewarmed by peritoneal dialysis as opposed to external warming (9).

It is unlikely that the rate of deep-body warming achieved with microwave exposure in the present study could be attained with conventional techniques such as skin heating or irrigation of the thoracic region with warm fluids. To achieve an equivalent warming rate with nonmicrowave techniques would require a temperature gradient that would cause protein denaturation and cell death. Therefore, microwaves are useful because the energy can be deposited directly and does not depend on conductive and/or convective transfer of heat from warm to cool tissues.

A significant problem with microwave rewarming, as was encountered in this study, is the development of "hot spots" and subsequently, tissue burns. Hot spots are likely to occur during microwave exposure, especially when the subject is exposed to resonant frequencies (7). Tissues and organs with a poor blood circulation, such as bone and the cornea, are more vulnerable to microwave burns (8). Hence, hypothermic tissue with little or no circulation may be especially susceptable to hot spots. With appropriate measures to avoid concentrated depositions of energy such as shielding the vulnerable areas or by continually rotating the position of the animal in the microwave field, burns from microwave rewarming may be prevented. For example the latter method has been used to avoid hot spots during the rewarming of frozen organs (5).

The present study has shown that whole-body microwave exposure at a resonant frequency is a feasible means of rapidly rewarming mammals from hypothermia. A major goal was to discern the maximum rate of warming that mice could safely tolerate. However, in this study a lethal heating rate was never reached.

It is of significance that the hypothermic mouse can tolerate a warming rate of at least 0.65°C/sec which is 17 to 200 times higher than other forms of rewarming including localized microwave exposure to the chest, warm water immersion, and natural recovery from hibernation (Table 1). A mouse immersed in a 37°C water bath rewarms at a rate of 0.037°C/sec. Assuming

TABLE 1
Comparison of Deep-Body Warming Rates during Recovery from Hypothermia with Various Types of Natural and Experimental Techniques

Species	Mode of rewarming	Rate of warming (°C/s)	Authors
Dog	Peritoneal dialysis	0.001	Patton and Doolittle (9)
Ground squirrel	Recovery from hibernation	0.003	Wang (12)
Rat	40°C water immersion	0.01	Andjus *et al.* (2)
Rat	3000 MHz over thorax	0.013	Andjus *et al.* (2)
Mouse	37°C water immersion	0.037	Gordon, unpublished[a]
Mouse	Whole-body 2450-MHz exposure	0.65	Gordon, present study

[a] Measurement made using dead animals.

linearity, to achieve a warming rate of 0.65°C/sec would require a water bath temperature of 650°C. Thus, internal energy deposition of electromagnetic radiation permits tremendously faster recovery rates from hypothermia.

SUMMARY

Twenty- to forty-gram mice cooled to colonic temperatures of 17 to 30°C were rewarmed to normothermia by exposure to whole-body 2450-MHz microwave radiation. Eighteen of nineteen mice survived rewarming at rates of 0.04 to as high as 0.65°C/sec. Hot spots from microwaves exposure, as indicated by deep tissue burns, were found at the base of the tail in 12 of 19 animals. The maximum rate of rewarming in these experiments (0.65°C/s) is much higher than warming rates achieved with external warming techniques such as immersion in warm water (~0.03°C/s). It is concluded that when care is taken to avoid hot spots, whole-body microwave exposure at resonant wavelengths may be a potential means for rapidly rewarming experimental animals from hypothermia.

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This paper has been reviewed by the health effects research laboratory, U.S. Environmental Protection Agency, and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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